

WHAT IS CLAIMED:

1. An isolated nucleic acid molecule selected from the group consisting of:

a) a nucleic acid molecule comprising a nucleotide sequence which is at least 80% identical to the nucleotide sequence of SEQ ID NO:1, 3, 5 or 6 or a fragment thereof;

b) a nucleic acid molecule comprising a sequence that hybridizes under high stringency conditions to a nucleic acid sequence consisting of SEQ ID NO:1, 3, 5 or 6, or its complement thereof;

c) a nucleic acid molecule that encodes a polypeptide at least 80% identical to the polypeptide of SEQ ID NO: 2 or 4; and

d) a fragment of (a), (b) or (c) at least 20 nucleotides in length.

2. A vector comprising the nucleotide molecule of claim 1.

3. A host cell harboring the nucleic acid molecule of claim 1.

4. The host cell of claim 3, wherein the host cell is a mammalian cell.

5. The host cell of claim 3, wherein the host cell is a human cell.

6. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:10, or its complement, wherein the nucleic acid includes nucleotides 203 and 204 (CA) of SEQ ID NO:10, or the complement thereof.

7. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:12, or its complement, wherein the nucleic acid includes nucleotide 201 (G) of SEQ ID NO:12, or the complement thereof.

8. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:14, or its complement, wherein the nucleic acid includes nucleotide 201 (G) of SEQ ID NO:14, or the complement thereof.

9. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:16, or its complement, wherein the nucleic acid includes 201 (G) of SEQ ID NO:16, or the complement thereof.

5

10. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:18, or its complement, wherein the nucleic acid includes nucleotide 201 (C) of SEQ ID NO:18, or the complement thereof.

10 11. The nucleic acid of claim 10, wherein the nucleic acid comprising at least 50 contiguous nucleotides of SEQ ID NO:20, or its complement, wherein the nucleic acid includes nucleotides 199 to 202 (GCCC) of SEQ ID NO:20, or the complement thereof.

15 12. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:20, or its complement, wherein the nucleic acid includes nucleotides 199 to 202 (GCCC) of SEQ ID NO:20, or the complement thereof.

20 13. The nucleic acid of claim 12, wherein the nucleic acid comprising at least 50 contiguous nucleotides of SEQ ID NO:20, or its complement, wherein the nucleic acid includes nucleotides 199 to 202 (GCCC) of SEQ ID NO:20, or the complement thereof.

25 14. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:22, or its complement, wherein the nucleic acid includes nucleotide 201 (G) of SEQ ID NO:22, or the complement thereof.

15. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:24, or its complement, wherein the nucleic acid includes nucleotide 201 (G) of SEQ ID NO:24, or the complement thereof.

16. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:26, or its complement, wherein the nucleic acid includes nucleotide 201 (C) of SEQ ID NO:26, or the complement thereof.

5 17. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:28, or its complement, wherein the nucleic acid includes nucleotide 201 (T) of SEQ ID NO:28, or the complement thereof.

10 18. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:30, or its complement, wherein the nucleic acid includes nucleotide 201 (T) of SEQ ID NO:30, or the complement thereof.

15 19. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:32, or its complement, wherein the nucleic acid includes nucleotide 201 (A) of SEQ ID NO:32, or the complement thereof.

20 20. An isolated nucleic acid comprising at least 20 contiguous nucleotides of SEQ ID NO:34, or its complement, wherein the nucleic acid includes nucleotide 201 (C) of SEQ ID NO:34, or the complement thereof.

21. An isolated nucleic acid comprising at least 15 contiguous nucleotides of SEQ ID NO:36, or its complement, wherein the nucleic acid includes nucleotide 201 (T) of SEQ ID NO:36, or the complement thereof.

25 22. A nucleic acid probe or primer comprising at least 15 contiguous nucleotides of SEQ ID NO:1, 3, 5 or 7.

30 23. An isolated polypeptide comprising a sequence at least 80% identical to the amino acid sequence of SEQ ID NO: 2 or 4, or a fragment thereof comprising at least 15 contiguous amino acids.

24. A fusion protein comprising the polypeptide of claim 23.

25. An antibody which selectively binds to the polypeptide of claim 23.

5 26. A method of producing a polypeptide, the method comprising culturing the host cell of claim 3 under conditions in which the nucleic acid molecule is expressed.

 27. A method of determining if a subject is at risk for type 2 diabetes, the method comprising evaluating the level, activity, expression and/or genotype of a T2DM-1 or T2DM-2
10 molecule in a subject, thereby determining if a subject is at risk for type 2 diabetes.

 28. The method of claim 27, further comprising diagnosing a subject as being at risk for or having type 2 diabetes.

15 29. The method of claim 27, wherein the method comprises detecting, in a biological sample of the subject, the presence or absence of a mutation in a T2DM-1 or T2DM-2 gene.

 30. The method of claim 27, wherein the method comprises detecting the presence or absence of a T2DM-1 or T2DM-2 polymorphism in the subject's T2DM-1 or T2DM-2 gene.
20

 31. The method of claim 30, wherein the polymorphism is selected from a polymorphism shown in FIG. 4 and FIG. 10.

 32. The method of claim 27, wherein the determining step comprises amplifying at least
25 a portion of a T2DM-1 or T2DM-2 nucleic acid molecule of the subject.

 33. The method of claim 27, wherein the determining step comprises sequencing at least a portion of a T2DM-1 or T2DM-2 nucleic acid molecule of the subject.

34. The method of claim 27, wherein the determining step comprises hybridizing a T2DM-1 or T2DM-2 nucleic acid molecule of the subject with a probe or primer described herein.

5 35. An array of nucleic acid molecules capable of detecting a T2DM-1 or T2DM-2 polymorphism described herein.

36. A set of oligonucleotides comprising a plurality of oligonucleotides, each of which is at least 70% complementary to a T2DM-1 or T2DM-2 nucleic acid.

10 37. A method of evaluating a subject, the method comprising:
providing a nucleic acid sample from the subject;
evaluating a genotype of the T2DM-1 or T2DM-2 gene of the subject; and
providing a determination of the subject's susceptibility to type 2 diabetes.

15 38. A method of identifying a T2DM-1 or T2DM-2 allele in a subject, the method comprising: identifying the presence or absence of two or more polymorphisms in the T2DM-1 or T2DM-2 gene of the subject

20 39. A method of treating a subject, the method comprising modulating the expression, level, or activity of a T2DM-1 or T2DM-2 molecule in the subject.

40. The method of claim 39, wherein the subject is identified as having or being at risk for type 2 diabetes an associated condition.

25 41. The method of claim 39, wherein T2DM-1 or T2DM-3 expression, level or activity is increased in the subject.

30 42. A method of screening for a compound that affects type 2 diabetes susceptibility, the method comprising:
providing a T2DM-1 or T2DM-2 protein or nucleic acid;

contacting the T2DM-1 or T2DM-2 protein or nucleic acid with a test compound, and determining if the test compound modulates the T2DM-1 or T2DM-2 protein or nucleic acid.

5 43. The method of claim 42, wherein the method includes

(1) providing a genetically engineered cell, tissue, or subject, comprising a nucleic acid that encodes a reporter molecule functionally linked to a control region of a T2DM-1 or T2DM-2 gene;

(2) contacting the cell, tissue or subject with a test agent; and

10 (3) evaluating a signal produced by the reporter molecule, the presence or strength of which is correlated with the effect of the test agent on the T2DM-1 or T2DM-2 control region.

44. The method of claim 42, further comprising administering the test compound to an experimental animal.

15

45. A transgenic non-human mammal comprising a T2DM-1 or T2DM-2 transgene.